Epidemiological evidence on glyphosate and adverse pregnancy outcomes.

Francisco J.R. Paumgartten

National School of Public Health - FIOCRUZ

Rio de Janeiro, RJ 21040-361, Brazil

Roundup and birth defects

Is the public being kept in the dark?

Michael Antoniou
Mohamed Ezz El-Din Mostafa Habib
C.Vyvyan Howard
Richard C. Jennings
Carlo Leifert
Rubens Onofre Nodari
Claire Robinson
John Fagan

Earth Open Source
June 2011

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Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling

Alejandra Paganelli, Victoria Gnazzo, Helena Acosta, Silvia L. López, and Andrés E. Carrasco*

Laboratorio de Embriología Molecular, CONICET-UBA, Facultad de Medicina, Universidad de Buenos Aires, Paraguay 2155, 3° piso (1121), Ciudad Autónoma de Buenos Aires, Argentina

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human health. Reports of neural defects and craniofacial malformations from regions where glyphosate-based herbicides (GBH) are used led us to undertake an embryological approach to explore the effects of low doses of glyphosate in development. *Xenopus laevis* embryos were incubated with 1/5000 dilutions of a commercial GBH. The treated embryos were highly abnormal with marked alterations in cephalic and neural crest development and shortening of the anterior−posterior (A-P) axis. Alterations on neural crest markers were later correlated with deformities in the cranial cartilages at tadpole stages. Embryos injected with pure glyphosate showed very similar phenotypes. Moreover, GBH produced similar effects in chicken embryos, showing a gradual loss of rhombomere domains, reduction of the optic vesicles, and

with the inhibition of *otx2* expression and with the disruption of cephalic neural crest development. The direct effect of glyphosate on early mechanisms of morphogenesis in vertebrate embryos opens concerns about the clinical findings from human offspring in populations exposed to GBH in agricultural fields.

Environmental & Analytical
Toxicology

Antoniou et al., J Environ Anal Toxicol 2012, S:4
http://dx.doi.org/10.4172/2161-0525.S4-006

Review Article Open Access

Teratogenic Effects of Glyphosate-Based Herbicides: Divergence of Regulatory Decisions from Scientific Evidence

M Antoniou[1], MEM Habib[2], CV Howard[3], RC Jennings[4], C Leifert[5], RO Nodari[6], CJ Robinson[7]* and J Fagan[8]*

[1]Head, Gene Expression and Therapy Group, Department of Medical and Molecular Genetics, King's College London School of Medicine, UK
[2]Professor of entomology, former director, Institute of Biology, UNICAMP, and former provost of extension and community affairs, UNICAMP, São Paulo, Brazil
[3]Professor, Centre for Molecular Biosciences, University of Ulster, Northern Ireland
[4]Affiliated research scholar, Department of History and Philosophy of Science, University of Cambridge, UK
[5]Research development professor for ecological agriculture at the University of Newcastle, UK. Interests: director and trustee of the Stockbridge Technology Centre Ltd (STC), UK
[6]Professor, Center for Agricultural Sciences (department of plant science), Federal University of Santa Catarina, Brazil
[7]Research director, Earth Open Source, London, UK. Interests: editor, GM Watch, UK
[8]Director, Earth Open Source. Interests: employed at a GMO testing and certification company

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REVIEW ARTICLE

Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance

Anthony SAMSEL [1] and Stephanie SENEFF [2]

[1] *Independent Scientist and Consultant, Deerfield, NH 03037, USA*
[2] *Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge, MA, USA*

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these amino acids. Celiac disease patients have an increased risk to non-Hodgkin's lymphoma, which has also been implicated in glyphosate exposure. Reproductive issues associated with celiac disease, such as infertility, miscarriages, and birth defects, can also be explained by glyphosate. Glyphosate residues in wheat and other crops are likely increasing recently due to the growing practice of crop desiccation just prior to the harvest. We argue that the practice of "ripening" sugar cane with glyphosate may explain the recent surge in kidney failure among agricultural workers in Central America. We conclude with a plea to governments to reconsider policies regarding the safety of glyphosate residues in foods.

Glyphosate and adverse pregnancy outcomes in humans

⇒Analytic epidemiological studies

→ Glyphosate-based herbicides

→ Unspecified pesticides in areas of intensive GM soy planting

(Study by Benítez-Leite et al, 2007)

⇒Reports of high incidence of birth defects in GM-soy areas

→ (Study by Campaña et al, 2010)

→ (Investigation Committee Report, Chaco province, Argentina, 2010)

Analytic epidemiological studies

Glyphosate-based herbicides *vs* birth defects
abortions
sex ratios
time-to-pregnancy

Search ($\rightarrow$ April 30, 2014):

Medline / toxline (pubmed)
LILACS – Latin American and the Caribean Health Literature

English / Spanish / Portuguese terms

Glyphosate *vs* **birth defects** (Analytic studies)

01 retrospective cohort + 03 case-control studies

Study	Exposure Assessment	Outcome (Birth defect)
Retrospective cohort Pesticide appliers Minnesota US [Garry et al, 2002]	**Interview** on pesticide use on job activities	**ADHD**: Attention Deficit Hyperactivity Disorder OR (95%CI) = **3.6 (1.3-9.6)**
Case-control Rural population California US [Rull et al, 2006]	Interview - **questionnaire** **Residential proximity** to sprayed fields (<1,000m) Early pregnancy	**NTDs: Neural Tube Defects** OR (95%CI) = **1.5 (1.0-2.4)** OR (95%CI) = **1.5 (0.8-2.9)+** +Logistic.Reg w/ multiple pesticides
Case-control Rural population California US [Yang et al, 2014]	Interview - **questionnaire** **Residential proximity** to sprayed fields (<1,000m) Peri-conception period	NTDs and oral clefts **Anencephaly: 0.9 (0.5-1.9)** **Spina bifida: 0.9 (0.5-1.4)** **CL w/wo CP : 0.9 (0.5-1.4)** **CP alone: 0.9 (0.5-1.5)**
Case-control Rural population California US [Carmichael et al, 2013]	Interview - **questionnaire** **Residential proximity** to sprayed fields (<1,000m) Early pregnancy (1-14 wks)	**Hypospadias** OR (95%CI) = **0.88 (0.48-1.64)**

Glyphosate *vs* **abortion** (Analytic studies)

01 retrospective cohort + 01 case-control study

Abortions, Pre-term births, Small for Gestational Age babies

Study	Exposure Assessment	Outcome
Retrospective cohort Rural population Ontario CA [Savitz et al, 1997]	Interview –questionnaire Paternal exposure	OR (95% CI) Abortion (Crop): 1.5 (0.8-2.7) (Yard): 1.4 (0.7-2.8) Pre-term (Crop): 2.4 (0.8-7.9) SGA (Crop): 0.8 (0.2-2.3)
Case-control Rural population, farmers Ontario CA [Arbuckle et al, 2001]	Interview – questionnaire Residential proximity to sprayed crops (within 500 m radius) Early pregnancy (1-98 d Pos Cpt, 1-14 wks embryonic age)	PreCpt *vs* late ab 1.7 (1.0-2.9) PreCpt *vs* early ab 1.1 (0.7-1.9) PosCpt *vs* ab (any gest age) 1.1 (0.7-1.7)

Glyphosate *vs* "**time-to-pregnancy**" (Analytic studies)

02 retrospective cohort studies

Curtis et al (1999) Rural Ontario CA,

Sanin et al (2014) Colombia (aerial spraying for eradication of illicit crops)

Delayed TTP not consistently associated with glyphosate exposure

- **Six epidemiology analytical studies** investigated a possible association between maternal/paternal exposure to glyphosate and adverse outcomes of pregnancy including birth defects. Two additional studies evaluated effects of glyphosate on time-to-pregnancy in fertile women.

- In most reviewed studies **exposure** was a categorical variable (exposed / not exposed) **assessed by maternal interviews (questionnaires).**

- Data from epidemiology studies provided **no consistent evidence of association** between **glyphosate** and **birth defects**, **abortions**, altered **sex ratios**, or delayed **time-to-pregnancy**

Studies and reports on the incidence of **birth defects** in **GM soy** areas in **South America**

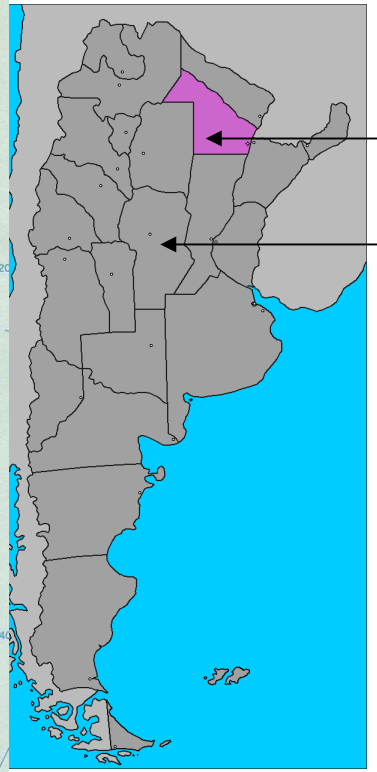
Benítez-Leite et al (2007) cases-control study Itapúa - Paraguay

Campaña et al (2010) incidences of 27 BDs in 9 regions of Argentina (Córdoba region - Argetina)

Investigation Committee report Chaco province - Argentina (2010)

Paraguay

- Itapúa



Argentina

- Chaco
- Córdoba

Pesticides *vs* birth defects

Malformaciones congénitas asociadas a agrotóxicos

Congenital Malformations Associated with Toxic Agricultural Chemicals

Benítez-Leite S[1], Macchi[1] ML, Acosta M[2].

1. Cátedra de Pediatría. Centro Materno Infantil (CMI). Facultad de Ciencias Médicas. UNA-Paraguay.
2. Hospital Regional de Encarnación – Paraguay.
Solicitud de sobretiros: rcorvalan@click.com.py

Esta investigación se realizó en el marco de la convocatoria 2006 para proyectos de investigación de la Dirección General de Investigaciones Científicas y Tecnológicas de la Universidad Nacional de Asunción.

Regional hospital of Encarnación
Department of Itapúa- Paraguay

Case-Control study

Cases: All neonates with single ou multiple malformations born at the Regional hospital of Encarnación – Paraguay

Controls: The next two healthy neonates (without malformations) of the same sex born at the hospital.

(exceptionally only one control child was included for a case)

Period: March 2006 to February 2007

Exposure assessment

Pesticide exposure and other relevant data were obtained by interview and maternal responses to a questionnaire.

Interviewers (data gatherers): internal doctors and nurses

Categorical variable: exposed / not exposed (no stratification)

Individual pesticides not identified (“pesticides”)

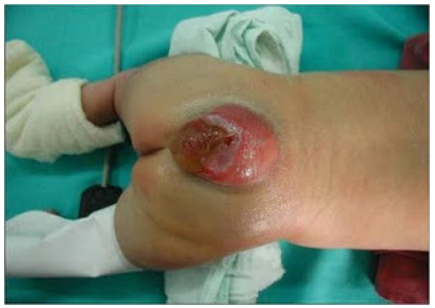


Table 2. Case-control study by Benitez-Leite et al (2007): Congenital malformations diagnosed in newborn cases.

	N	%
Congenital asplenia (absence of spleen)	1	1.9
Congenital absence of the hand	1	1.9
Congenital absence of the ear	2	3.8
Anencephaly	2	3.8
Aplasia cutis congênita - pre-auricular tags	1	1.9
Pre-auricular tags	6	11.5
Abnormal facies	6	11.5
Microcephaly-craniosynostosis-turricephaly	1	1.9
Cryptorchidism	1	1.9
Cloacal exstrophy	1	1.9
Pre-auricular fistula /coloboma auris	1	1.9
Cleft palate –bilateral club foot	1	1.9
Hydrocephalus	1	1.9
Hydrocephalus with frontal tumor	1	1.9
Hypospadias	1	1.9
Ear anomalies, synechiae, low set ears, pre-auricular tags	3	5.8
Multiple malformations	8	16.0
Myeolomeningocele	3	5.8
Club foot	4	7.7
Club foot and agenesis of toes	1	1.9
Polydactyly	4	7.7
Syndactyly	1	1.9
Total	**52**	**100**

Table 3. Case-control study by Benitez-Leite et al (2007): Data on the association between maternal exposure to pesticides and birth defects.

	cases	controls	OR (IC 95%)
Newborns (N)	52	87	
Maternal/paternal exposure assessment :			
1- Paternal exposure to pesticides	28.8 (15/52)	22.9 (20/87)	1.36 (0.57-3.20
2- Pesticides stored at home	**15.3 (8/52)**	**1.1 (1/87)**	**15.34 (1.96-701.63)**
3- Personal protective equipment when working with pesticides	7.8 (4/51)	10.5 (9/85)	0.72 (0.17-2.79)
4- Living nearby sprayed crops	**42.3 (22/52)**	**22.9 (20/87)**	**2.46 (1.09-5.57)**
Residential proximity to sprayed crops (<1,000 m)			**2.66 (1.19-5.97)**
5- Presence in sprayed fields before and during pregnancy	28.8 (15/52)	17.4 (15/86)	1.92 (0.78-4.74)
6- Meals in sprayed fields	11.5 (6/52)	3.4 (3/87)	3.62 (0.73-23.38)
7- Pesticide contaminated clothes washing (at home)	21.1 (11/52)	9.1 (8/87)	2.65 (0.89-8.00)
8- Direct and/or accidental contact with pesticides	19.2 (10/52)	6.8 (6/87)	3.19 (0.97-11.4)
9- Report of pesticide poisoning symptoms	19.2 (10/52)	9.1 (8/87)	2.35 (0.77-7.23)
10 - Re-use of empty pesticide containers for potable water	0 (0/52)	1.1 91/87)	-

Data from Benitez-Leite et al's study Tables 5 and 6 were combined. Interview questionnaires were responded by the mothers. It is unclear in M&M and results whether some questions (above) refer to the father, the mother or both parents.

Table 4. Case-control study by Benítez-Leite et al (2007): Major flaws in study design and data analysis.

1. Selection bias	Poor description in M&M of how the control group represents the cases, independent of the exposure (pesticides) being investigated.
2. Information bias	Recall bias mothers of malformed children (the cases) differ from mothers of healthy controls leading to misclassification. Data gatherer bias. Interviewers were aware of cases and control status and main research hypothesis.
3. Exposure assessment.	No quantitative assessment of exposure. Categorical (exposed / not exposed) assessment based on responses to imprecise questions. No stratification of levels of exposure.
4. Confounding factors (CF)	CFs were not minimized or eliminated in the design phase (by restriction or matching), nor were they handled in the data analysis phase (logistic regression).
5. Statistical power	Researchers did not estimate whether the study sample size provided adequate statistical power for comparisons, *i.e.*, >80% power for 10% change in OR at $P<0.05$.

Benítez-Leite et al‘ study: Examples of relevant Confounding Factors that were not controlled :

History of congenital malformation in the family:

Cases 25% (13/52) vs Controls 4.5% (4/87)

OR= 6.8 (1.94-30.56)

Fever during early pregancy: Cases 25.0% *vs* Controls 13.1%

Diseases during pregnancy: Cases 21.1% *vs* Controls 11.4%

Consumption of drugs during first trimester of pregnancy:

Cases 35.2 % *vs* 22.3%

Data from Tables 2 and 3 (Benítez-Leite et al, 2007).

- The **association between pesticides (in general) and birth defects reported by Benítez-Leite et al (2007) must be interpreted with caution** because study design and data analysis did not deal with possible confounding factors and selection and information biases

El articulo "***Malformaciones Congénitas Asociadas a Agrotóxicos***" publicado en la revista Pediatría en el Volumen 34 - Número 2 del año 2007 motivó un comentario periodístico publicado en el diario **ABC color, Asunción - Paraguay, el 5 de octubre del 2008 página 30.** Dada la importancia del tema, se presenta la respuesta de los autores:

En relación a los agrotóxicos, ante la duda, el derecho a la salud debe prevalecer

When in doubt about toxic agricultural chemicals, health rights must come first

Atte

Las autoras: Benítez-Leite S; Macchi ML; Acosta M.

En relación puntual al contenido del estudio, éste es un trabajo que investiga exposición a pesticidas y asociación con malformaciones congénitas y no precisamente exposición específica al glifosato utilizado en los cultivos de soja. Si fuere así, el diseño y la búsqueda de malformaciones se debería realizar en los pobladores expuestos directamente al glifosato, en los diferentes distritos de Encarnación y establecer comparaciones. En este caso, se escogió el hospital regional de Encarnación por la factibilidad y por estar en una zona eminentemente agrícola.

"...this work **studied pesticide exposure and association with congenital malformations and not** (exactly / specifically) **exposure to glyphosate used in soy crops**. If it were the case, the study design and the selection of cases of malformations should have involved individuals that were directly exposed to glyphosate in the different districts of Encanación so that comparions could be made."

Stella Benítez-Leite, Maria Macchi & Matilde Acosta, 2009.

Chaco Province Report 2010.

WATER POLLUTANTS INVESTIGATION COMMITTEE – FIRST REPORT

Introduction

This first report presents data on the current situation and considerations related to cancer (Ca) in children and newborn malformations.

Report from the 1st NATIONAL MEETING OF PHYSICIANS IN THE CROP-SPRAYED TOWNS

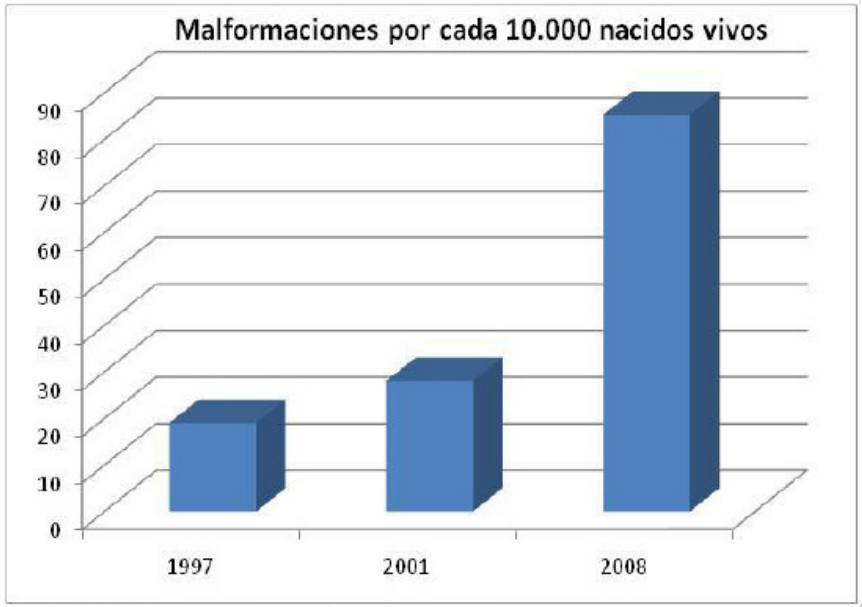
Faculty of Medical Sciences, National University of Cordoba.
August 27th and 28th 2010, University Campus, Cordoba

Coordinators: Dr. Medardo Ávila Vazquez, Prof. Dr. Carlos Nota.

Introduction

For nearly 10 years, the residents of rural and periurban areas, where agricultural activities are carried out based on the current model of agro-industrial production, have been demanding to the political authorities, the courts of justice, and also protesting before the general public, because they feel that the health of their communities is being environmentally affected, mainly through sprayings of agrochemicals used for different types of agricultural crops, but also for the handling and storage of these chemicals in populated areas, the waste disposal, as well as the collection of grains soaked with chemicals within the towns.

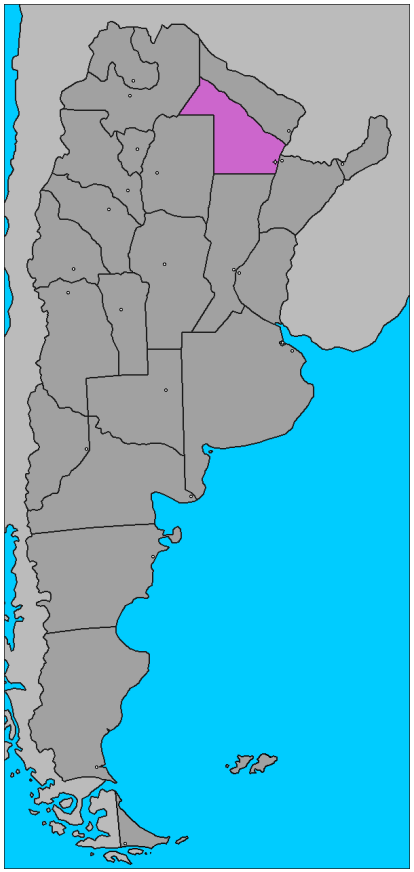
The rate of birth defects in 10,000 live births showed a significant increase in recent years, as shown in Graph No. 1.



Birth defects per 10,000 live births

Soy-growing area, Chaco. 1969/70 to 2008/09 Series (in ha)

Graph No. 1: Number of congenital birth defects per 10,000 live births, Neonatal Unit, Hospital Perrando, Resistencia; and evolution of Soy-growing areas in the Province of Chaco



Chaco Province

Hospital Julio Perrando
Resistencia - Chaco

Hospital Julio Perrando
Neonatal Unit

"Incidence" = Hospital Perrando records of birth defects
/population registry of births in the region

The reported ratios are not reliable estimates of incidence of Birth Defects in the local population.

Table 5. Data on the incidence of birth defects in the area of La Leonese and Las Palmas reported by the Water Pollutants Investigation Committee, Chaco Province, Argentina, 2010.

Year (12 mo)	Malformed children (Neonatal Dept of Hospital Perrando records) (N)	Births in the region (population registry) (N)	Birth defects rates in the region (per 10,000 births)
1997-8	46	24,030	19.1
2001-2	60	21,339	28.1
2008-9	186	21,808	85.3

A study of birth defects in seven regions of Argentina found that Cordoba, an area of intensive planting of GM soy where pesticides are heavily used, had a higher incidence of spina bifida, microtia, cleft lip with cleft palate, polycystic kidney, postaxial polydactyly and Down's syndrome than other regions [68]. Many of these defects are of the type associated with disturbances in the retinoic acid signalling pathway, though it is not possible to identify a sole causative agent.

Antoniou et al, 2011

Arch Argent Pediatr 2010;108(5):409-417 / 409

Prevalencia al nacimiento de 27 anomalías congénitas seleccionadas, en 7 regiones geográficas de la Argentina

Births prevalence of 27 selected congenital anomalies in 7 geographic regions of Argentina

Dra. Hebe Campaña[a], Lic. Mariela S. Pawluk[a], Dr. Jorge S. López Camelo[a,b] y Grupo de Estudio del ECLAMC[c]

TABLA 2. *Veintisiete anomalías congénitas en siete regiones de la Argentina durante el período 1994-2007, sus tasas/10 000 (IC al 95%)*

Región	MET	PAM	CEN	CUY	NEA	NOA	PAT	TOTAL
Anomalía	**Tasa (IC 95%)**	**Tasa (IC 95%)**	**Tasa (IC 95%)**	**Tasa (IC 95%)**	**Tasa (IC 95%)**	**Tasa (IC 95%)**	**Tasa (IC 95%)**	**Tasa (IC 95%)**
Onfalocele	3,1 (2,5-3,9)	1,5 (0,9-2,3)	3,0 (2,0-4,2)	2,2 (1,3-3,6)	2,9 (1,7-4,5)	3,8 (3,0-4,8)	3,8 (1,6-7,4)	2,9 (2,5-3,3)
Gastrosquisis	3,8 (3,1-4,7)	2,6 (1,9-3,5)	4,4 (3,2-5,8)	3,0 (1,9-4,5)	4,3 (2,8-6,3)	4,1 (3,3-5,2)	4,2 (1,9-8,1)	3,7 (3,3-4,1)
Anencefalia	10,3 (9,1-11,7)	5,1 (4,0-6,3)	7,9 (6,3-9,8)	4,6 (3,2-6,4)	4,3 (2,8-6,3)	8,3 (7,1-9,8)	4,7 (2,3-8,7)	7,5 (6,9-8,1)
Espina bífida	13,2 (11,8-14,7)	7,5 (6,2-9,0)	12,1 (10,1-14,3)	7,1 (5,3-9,2)	5,4 (3,8-7,6)	10,0 (8,6-11,5)	2,8 (1,0-6,2)	9,9 (9,2-10,6)
Hidrocefalia	12,5 (11,2-14,0)	10,8 (9,3-12,5)	12,8 (10,8-15,1)	6,6 (5,0-8,8)	9,8 (7,5-12,5)	10,9 (9,4-12,5)	10,4 (6,5-15,7)	11,1 (10,4-11,8)
Cefalocele	3,5 (2,8-4,3)	1,5 (0,9-2,2)	3,0 (2,0-4,2)	2,2 (1,3-3,6)	1,4 (0,7-2,7)	2,8 (2,1-3,7)	0,0 (0,0-1,7)	2,5 (2,2-2,9)
Microtia	5,3 (4,5-6,3)	3,4 (2,6-4,4)	5,4 (4,1-7,0)	3,5 (2,3-5,1)	2,7 (1,6-4,4)	4,6 (3,6-5,7)	3,8 (1,6-7,4)	4,4 (4,0-4,9)
Labio leporino	4,3 (3,5-5,2)	2,8 (2,0-3,7)	3,4 (2,4-4,7)	4,2 (2,9-5,9)	1,6 (0,7-2,9)	4,1 (3,2-5,1)	6,6 (3,6-11,1)	3,7 (3,3-4,1)
Labio leporino con paladar hendido	9,8 (8,5-11,1)	8,2 (6,9-9,7)	12,1 (10,1-14,3)	10,6 (8,4-13,2)	9,9 (7,6-12,7)	11,7 (10,2-13,4)	9,9 (6,1-15,1)	10,2 (9,6-11,0)
Paladar hendido	5,6 (4,7-6,7)	4,0 (3,1-5,1)	4,8(3,6-6,3)	3,7 (2,4-5,3)	3,0 (1,8-4,7)	4,7 (3,8-5,8)	6,1 (3,3-10,5)	4,7 (4,2-5,2)
Atresia esofágica	4,0 (3,3-4,9)	3,9 (3,0-4,9)	5,2 (3,9-6,8)	3,5 (2,3-5,1)	3,4 (2,1-5,1)	3,3 (2,5-4,2)	2,4 (0,8-5,5)	3,8 (3,4-4,3)
Atresia anorrectal	6,0 (5,1-7,1)	4,3 (3,4-5,5)	7,0 (5,5-8,7)	3,3 (2,1-4,8)	5,9 (4,2-8,2)	7,2 (6,1-8,6)	5,7 (2,9-9,9)	5,8 (5,3-6,4)
Cardiopatía troncal	6,5 (5,5-7,6)	5,4 (4,4-6,7)	5,8 (4,5-7,5)	5,0 (3,5-6,8)	0,05 (0,0-0,1)	3,9 (3,0-4,9)	4,7 (2,3-8,7)	5,0 (4,5-5,5)
CIA	4,8 (4,0-5,8)	3,0 (2,2-4,0)	0,7 (0,3-1,3)	1,3 (0,6-2,4)	1,6 (0,8-2,9)	2,5 (1,8-3,3)	7,1 (4,0-11,7)	2,9 (2,6-3,3)
CIV	15,1 (13,6-16,8)	15,1 (13,3-17,2)	7,1 (5,6-8,8)	8,9 (6,9-11,3)	1,9 (1,0-3,4)	12,2 (10,7-13,9)	18,4 (13,1-25,1)	12,0 (11,3-12,8)
Genital ambiguo	1,6 (1,2-2,2)	1,1 (0,7-1,7)	1,6 (0,9-2,5)	1,4 (0,7-2,6)	1,8 (0,9-3,1)	2,1 (1,5-2,9)	1,4 (0,3-4,1)	1,6 (1,4-1,9)
Hipospadias graves	3,7 (3,0-4,6)	6,5 (5,3-7,8)	2,8 (1,9-4,0)	2,6 (1,6-4,0)	1,7 (0,9-3,1)	1,5 (1,0-2,1)	0,9 (0,1-3,1)	3,3 (3,0-3,7)
Agenesia renal	3,5 (2,8-4,3)	1,6 (1,0-2,3)	3,9 (2,8-5,3)	1,2 (0,5-2,2)	2,7 (1,6-4,4)	1,6 (1,1-2,3)	2,8 (1,0-6,2)	2,5 (2,2-2,9)
Poliquistosis renal	4,7 (3,8-5,6)	3,2 (2,4-4,2)	4,5 (3,4-6,0)	2,1 (1,2-3,4)	1,3 (0,6-2,5)	2,1 (1,5-2,8)	3,8 (1,6-7,4)	3,3 (2,9-3,7)
Hidronefrosis	5,0 (4,1-5,9)	6,3 (5,1-7,6)	4,5 (3,4-6,0)	2,0 (1,1-3,2)	3,5 (2,2-5,3)	5,6 (4,6-6,8)	2,8 (1,0-6,2)	4,9 (4,4-5,4)
Polidactilia postaxial	11,3 (10,0-12,7)	9,3 (7,9-11,0)	14,5 (12,3-16,9)	13,2 (10,8-16,0)	12,3 (9,7-15,4)	10,3 (8,9-11,9)	6,1 (3,3-10,5)	11,2 (10,5-11,9)
Polidactilia preaxial	3,8 (3,1-4,7)	3,6 (2,7-4,7)	4,2 (3,0-5,6)	3,1 (2,0-4,7)	2,1 (1,1-3,6)	4,2 (3,3-5,2)	2,4 (0,8-5,5)	3,7 (3,3-4,1)
Reducción transversal terminal	3,5 (2,8-4,3)	3,1 (2,3-4,0)	2,2 (1,4-3,3)	3,1 (2,0-4,7)	3,2 (2,3-4,9)	3,0 (2,3-3,9)	1,9 (0,5-4,8)	3,0 (2,7-3,4)
Reducción longitudinal preaxial	2,2 (1,7-2,9)	1,3 (0,8-2,0)	1,5 (0,8-2,4)	1,0 (0,5-2,1)	1,1 (0,5-2,3)	1,4 (0,9-2,1)	1,0 (0,3-4,1)	1,8 (1,3-1,9)
Hernia diafragmática	4,4 (3,6-5,3)	4,6 (3,6-5,7)	4,5 (3,3-5,9)	2,7 (1,7-4,2)	2,1 (1,1-3,6)	4,3 (3,4-5,4)	5,2 (2,6-9,3)	4,1 (3,7-4,6)
Agenesia pectoral	1,0 (0,6-1,4)	1,2 (0,7-1,8)	0,7 (0,3-1,3)	0,9 (0,4-1,9)	0,3 (0,0-1,2)	1,3 (0,8-1,9)	0,5 (0,0-2,6)	1,0 (0,8-1,2)
Síndrome de Down	21,9 (20,1-23,9)	19,1 (17,0-21,3)	21,4 (18,8-24,4)	16,4 (13,6-19,5)	20,5 (17,1-24,3)	18,1 (16,2-20,2)	12,3 (8,0-18,0)	19,6 (18,7-20,6)

NEA: Chaco, Formosa, Misiones

CEN: Córdoba

MET: Buenos Aires

ECLAMC network hospitals

Campaña et al, 2010

27 congenital anomalies in 7 Argentinean regions, 1994-2007, /10 000 (95% CI)

Región	MET	CEN	NEA	TOTAL
Anomalía	Tasa (IC 95%)	Tasa (IC 95%)	Tasa (IC 95%)	Tasa (IC 95%)
Onfalocele	3,1 (2,5-3,9)	3,0 (2,0-4,2)	2,9 (1,7-4,5)	2,9 (2,5-3,3)
Gastrosquisis	3,8 (3,1-4,7)	4,4 (3,2-5,8)	4,3 (2,8-6,3)	3,7 (3,3-4,1)
Anencefalia	10,3 (9,1-11,7)	7,9 (6,3-9,8)	4,3 (2,8-6,3)	7,5 (6,9-8,1)
Espina bífida	13,2 (11,8-14,7)	12,1 (10,1-14,3)	5,4 (3,8-7,6)	9,9 (9,2-10,6)
Hidrocefalia	12,5 (11,2-14,0)	12,8 (10,8-15,1)	9,8 (7,5-12,5)	11,1 (10,4-11,8)
Cefalocele	3,5 (2,8-4,3)	3,0 (2,0-4,2)	1,4 (0,7-2,7)	2,5 (2,2-2,9)
Microtia	5,3 (4,5-6,3)	5,4 (4,1-7,0)	2,7 (1,6-4,4)	4,4 (4,0-4,9)

MET: Buenos Aires + surroundings

CEN: Córdoba

NEA: Chaco + Formosa+ Misiones provinces

Córdoba

Chaco

Rates= (Neonates with a CA) / (Neonates born at the hospitals)

- There is no consistent data indicating that in South American regions of extensive planting of GM soy (where glyphosate is intensively used) there is a higher incidence of birth defects.

In conclusion, **data from** available **epidemiology studies** – except for a possible association with attention deficit hyperactivity disorder – **do not support current public concerns on the developmental toxicity of glyphosate**.

Thank you !!!